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# Asymptotic results on a class of adaptive multi-treatment designs<sup>☆</sup>

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## Abstract

The play-the-winner (PW) rule is an important method in clinical trials where patients can be assigned to one of the two treatments. In the PW rule, the probability of the next patient to be assigned to a particular treatment only depends on the response of the current patient. In this paper, we consider a general kind of PW rule for multi-treatment adaptive designs, in which the probability that a treatment is assigned to the next patient depends upon both the response of the previous patient and an estimated parameter, e.g., the observed success rate. Using this kind of adaptive designs, more information of previous stages are used to update the model at each stage, and more patients may be assigned to better treatments. The strong consistency and the asymptotic normality are established for the allocation proportions.

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## 1. Introduction

In comparing treatments 1 and 2 with dichotomous response (success and failure), suppose subjects arrive to the experiment sequentially and must be assigned immediately to treatment 1 or 2. Zelen [18] proposed the well-known play-the-winner (PW) rule: *a success*

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on a particular treatment generates a future trial on the same treatment with a new patient. A failure on a treatment generates a future trial on the alternate treatment. The PW rule is used for the ethical consideration in which more patients are assigned to a better treatment. As an extension of PW rule, Wei and Durham [17] proposed the randomized play-the-winner (RPW) rule based on the urn model. Wei [16] extended the RPW rule to multi-treatment clinical trials. And he also defined a generalized Polya's urn (GPU) design. The asymptotic properties of the RPW rule and its various generalizations to multi-treatment cases based on the GPU have been studied by many authors (cf., [16,14,13,2,3], etc.). Recently, Bai et al. [4] proposed a new adaptive design for multi-arm clinical trials. In this adaptive design, the urn is updated according to the rate of sample's success. Such design can assign more patients to better treatments than Wei's does. However, the asymptotic distribution of the allocation proportion is unknown.

When the cure rate of each treatment is large (close to 1), the asymptotic distribution of the allocation proportion is unknown in using the RPW rule or its generalizations to multi-treatment cases based on the GPU. The variability of the RPW rule and the GPU model is very high unless all treatments have low cure rates. The variability of allocation may have a strong effect on the power. This has been demonstrated by the simulation studies of Melfi and Page [9] as well as Rosenberger et al. [12], and Hu and Rosenberger [8]. Due to the unknown distribution and high variability, the designs in which we use urn models become less applicable when the treatments have high cure rates, in sense that it is difficult to test whether or not a design truly assign more patients to better treatments or the design fit the desirable goals.

In this paper, we consider an alternative generalization of the PW rule and define a new adaptive design. In this new adaptive design, instead of using the urn model, we assign each patient directly with a certain probability that depends on an estimated parameter, e.g., the observed success rate. A special case (see Example 2.1) of this new adaptive design is similar to the one proposed by Bai et al. [4]. However, the asymptotic normality holds now in almost all cases. Another special case (see Example 2.3) is the sequential maximum likelihood procedure mentioned by Melfi and Page [9,10] and Melfi et al. [11]. In Section 2, we define the new design and give some examples. The asymptotic properties, including the strong consistency and its convergence rate, the asymptotic normality and Gaussian approximation are discussed in Section 3. The technical proofs are given in Section 4.

## 2. The design and examples

Consider a  $d$ -treatment clinical trial. Patients are recruited to the clinical trial sequentially and can respond immediately to treatments. Suppose at stage  $m$ , the  $m$ th patient is assigned to treatment  $i$ . We write the response of the  $m$ th patient to treatment  $i$  as  $\xi_{m,i}$ , which is a random variable following the distribution  $P_{\theta_i}$ , where  $\theta_i \in \Theta_i$ . Then the  $(m+1)$ th patient will be assigned to treatment  $j$  according to a certain probability, which depends on the response  $\xi_{m,i}$  of the  $m$ th patient. Let  $d_{ij}(\xi_{m,i})$  denote this probability. After  $n$  assignments, let  $N_{ni}$  be the number of patients assigned to treatment  $i$ , for  $i = 1, \dots, d$ , and let  $X_{ni} = 1$  if the  $n$ th patient is assigned to treatment  $i$  and 0 otherwise. Write  $\mathbf{N}_n = (N_{n1}, \dots, N_{nd})$ ,  $\mathbf{X}_n = (X_{n1}, \dots, X_{nd})$  and  $\boldsymbol{\theta} = (\theta_1, \dots, \theta_d)$ . It is obvious that  $\mathbf{N}_n \mathbf{1}' = N_{n1} + \dots + N_{nd} = n$ ,

where  $\mathbf{1} = (1, \dots, 1)$ . Also,

$$P(X_{m+1,j} = 1 | X_{m,i} = 1, \xi_{m,i}) = d_{ij}(\xi_{m,i}), \quad i, j = 1, \dots, d,$$

$$d_{ij}(\xi_{m,i}) \geq 0 \quad \text{and} \quad \sum_{j=1}^d d_{ij}(\xi_{m,i}) = 1.$$

Such a design is a generalization of the two-treatment Markov chain adaptive design proposed by Bai et al. [1]. We write  $\xi_m = (\xi_{m,1}, \dots, \xi_{m,d})$ , and assume that  $\{\xi_m, m = 1, 2, \dots\}$  is a sequence of i.i.d. random vectors. In the clinical trial,  $\xi_{i,k}$  is observed when the  $i$ th patient is assigned to treatment  $k$ , i.e.,  $X_{i,k} = 1$ . The complete data consist of all the responses  $\{\xi_{i,k}\}$ . The observed data are  $\{\xi_{i,k} : X_{i,k} = 1\}$ .

In many cases, the parameters  $\theta_k$ 's can be regarded as rules to measure whether a treatment is good or not. If  $\theta_1, \dots, \theta_d$  are known, it is reasonable to use them to optimize the design. In such case, the assignment probability  $d_{ij}$  depends on  $\theta$ , i.e.,

$$P(X_{m+1,j} = 1 | X_{m,i} = 1, \xi_{m,i}) = d_{ij}(\theta, \xi_{m,i}), \quad i, j = 1, \dots, d$$

and then

$$P(X_{m+1,j} = 1 | X_{m,i} = 1) = h_{ij}(\theta) =: E[d_{ij}(\theta, \xi_{m,i})], \quad i, j = 1, \dots, d.$$

It follows that  $\{\mathbf{X}_n; n \geq 1\}$  is a homogeneous Markov chain with transition matrix

$$\mathbf{H} = \mathbf{H}(\theta) = (h_{ij}(\theta))_{i,j=1}^d.$$

However, the parameter  $\theta$  is usually unknown and needs to be estimated. Now let us consider the following adaptive design. Throughout this paper, we assume that  $\theta = E\xi_m$ . Then we can use the sample mean to estimate  $\theta$ .

**Adaptive Design 1.** Suppose the previous  $m - 1$  patients are assigned and the responses are observed. Let  $\hat{\theta}_{m-1} = (\hat{\theta}_{m-1,1}, \dots, \hat{\theta}_{m-1,d})$  be an estimate of  $\theta$ , where  $\hat{\theta}_{m-1,k} = \frac{\sum_{i=1}^{m-1} X_{i,k} \xi_{i,k} + \theta_{0,k}}{N_{m-1,k} + 1}$ ,  $k = 1, \dots, d$ . Here,  $\theta_0 = (\theta_{0,1}, \dots, \theta_{0,d})$  is a known starting value.

Now, if the  $m$ th patient is assigned to treatment  $i$  and the response is observed, then we assign the  $(m + 1)$ th patient to treatment  $j$  with probability  $d_{ij}(\hat{\theta}_{m-1}, \xi_{m,i})$ ,  $j = 1, \dots, d$ . However, to insure that each treatment is tested by enough patients, i.e.,  $N_{ni} \rightarrow \infty$  a.s.,  $i = 1, \dots, d$ ,  $d_{ij}(\hat{\theta}_{m-1}, \xi_{m,i})$  could be modified by  $(1 - 1/m)d_{ij}(\hat{\theta}_{m-1}, \xi_{m,i}) + 1/md$  if necessary. That is

$$P(X_{m+1,j} = 1 | \mathcal{F}_m, X_{m,i} = 1, \xi_{m,i}) = \left(1 - \frac{1}{m}\right) d_{ij}(\hat{\theta}_{m-1}, \xi_{m,i}) + \frac{1}{md},$$

$$i, j = 1, \dots, d. \quad (2.1)$$

Here  $\mathcal{F}_n = \sigma(\mathbf{X}_1, \dots, \mathbf{X}_n, \xi_1, \dots, \xi_{n-1})$  is the history sigma field. We also let  $h_{ij}(\hat{\theta}_{m-1}) = E[d_{ij}(\hat{\theta}_{m-1}, \xi_{m,i}) | \mathcal{F}_{m-1}]$  and write  $\mathbf{H}(\hat{\theta}_{m-1}) = (h_{ij}(\hat{\theta}_{m-1}))_{i,j=1}^d$ .

**Remark 2.1.** *If*

$$\sum_{m=2}^{\infty} \min_i h_{ij}(\hat{\theta}_{m-1}) = \infty \text{ a.s., } j = 1, \dots, d, \quad (2.2)$$

then the modification of  $d_{ij}(\hat{\theta}_{m-1}, \xi_{m,i})$  is not necessary. For example, if  $\Theta =: \{\mathbf{x} : h_{ij}(\mathbf{x}) > 0, i, j = 1, \dots, d\}$  is a rectangle in  $\mathbb{R}^d$  of the form  $(\mathbf{a}, \mathbf{b})$ ,  $(\mathbf{a}, \mathbf{b}]$ , etc., and also  $\theta \in \Theta$ ,  $\hat{\theta}_{m-1} \in \Theta$  for each  $m$ , then (2.2) is satisfied (see the proof in Section 4).

**Remark 2.2.** *Usually, many cases, in which the parameter  $\theta$  is not a mean of the response  $\xi_n$ , can be transferred to the case we have studied above. In fact, if for each  $k$ , the estimator  $\theta_{n,k} = \hat{\theta}_{n,k}(\xi_{j,k} : j = 1, 2, \dots, n)$  of  $\theta$  can be written in the following form:*

$$\hat{\theta}_{n,k} = \frac{1}{n} \sum_{j=1}^n f_k(\xi_{j,k}) + o(n^{-1/2-\delta}) \text{ for some } \delta > 0 \text{ and functions } f_k, \quad (2.3)$$

then in the Adaptive Design 1, we can define

$$\hat{\theta}_{m-1,k} = \hat{\theta}_{n,k}(\xi_{j,k} : X_{j,k} = 1, j = 1, 2, \dots, m-1).$$

Many maximum likelihood estimators and moment estimators satisfy (2.3).

As a function of  $\hat{\theta}$ ,  $\mathbf{H}(\hat{\theta})$  is assumed to be continuous at  $\theta$ , i.e.,  $\mathbf{H}(\mathbf{x}) \rightarrow \mathbf{H} = \mathbf{H}(\theta)$  as  $\mathbf{x} \rightarrow \theta$ . It is obvious that  $\mathbf{H}\mathbf{1}' = \mathbf{1}'$ . So,  $\lambda_1 = 1$  is an eigenvalue of  $\mathbf{H}$ . Let  $\lambda_2, \dots, \lambda_d$  be other  $d-1$  eigenvalues of  $\mathbf{H}$ , and let  $\lambda = \max\{|\lambda_2|, \dots, |\lambda_d|\}$ . Then  $\lambda \leq 1$ . Also, we let  $\mathbf{v} = (v_1, \dots, v_d)$  be a left eigenvector of  $\mathbf{H}$  corresponding to its maximal eigenvalue  $\lambda_1 = 1$  with  $\mathbf{v}\mathbf{1}' = 1$  and  $v_i \geq 0, i = 1, \dots, d$ . Such an eigenvector according to the matrix theory is unique when  $\lambda_i \neq \lambda_1, i = 2, \dots, d$ . In the next section, we will claim that under some suitable conditions (stated in Section 3) on the function  $\mathbf{H}(\cdot)$  and moments of the responses,

$$\frac{\mathbf{N}_n}{n} \rightarrow \mathbf{v} \text{ a.s. and } n^{1/2} \left( \frac{\mathbf{N}_n}{n} - \mathbf{v} \right) \xrightarrow{\mathcal{D}} N(\mathbf{0}, \Lambda), \quad (2.4)$$

if  $\lambda < 1$ , where  $\Lambda$  is defined as in (3.4).

Next, we give some examples of the special case that the treatments have dichotomous outcomes, the success and failure. Consider that the patient is assigned to treatment  $k$ , let  $p_k$  be the probability of success, and  $q_k = 1 - p_k$ , for  $k = 1, \dots, d$ . We assume that  $0 < p_k < 1$ , for  $k = 1, \dots, d$ . As an extension of the PW rule to the multi-treatment case, Hoel and Sobel [6] proposed the cyclic play-the-winner (PWC) rule: *if the response on treatment  $k$  is a success, we assign the next patient to the same treatment. If the response is a failure, we assign the next patient to the treatment  $k+1$ . Here, treatment  $d+1$  means treatment 1.* By using the PWC rule, one has

$$\frac{N_{nk}}{n} \xrightarrow{P} v_i^{\text{PWC}} =: \frac{1/q_i}{\sum_{j=1}^d 1/q_j}, \quad i = 1, \dots, d. \quad (2.5)$$

The PWC rule can make more patients to undergo better treatments. However, one may argue, when there is a failure on treatment  $k$ , why we assign the next patient to treatment

$k + 1$  instead of any other treatment or some of the  $d - 1$  treatments with certain probabilities. When there is a failure on treatment  $k$ , it should be more reasonable to assign the next patient with higher probability to a better treatment among the other  $d - 1$  treatments. Motivated by this, we will consider the following adaptive design.

**Example 2.1.** If the response on treatment  $k$  is a success, we assign the next patient to the same treatment. If the response is a failure, we assign the next patient to other  $d - 1$  treatments with probabilities proportional to the estimated rate of success, i.e., at stage  $m$ , when the response of the  $m$ th patient on treatment  $k$  is a failure, we assign the  $(m + 1)$ th patient to treatment  $j$  with probability  $\frac{\hat{p}_{m-1,j}}{(M_{m-1} - \hat{p}_{m-1,k})}$  for all  $j \neq k$ , where  $M_{m-1} = \sum_{j=1}^d \hat{p}_{m-1,j}$ ,  $\hat{p}_{m-1,j} = \frac{S_{m-1,j}+1}{N_{m-1,j}+1}$ , and  $S_{m-1,j}$  denotes the number of successes of treatment  $j$  in all the  $N_{m-1,j}$  trials of previous  $m - 1$  stages,  $j = 1, \dots, d$ . For this design, we have

$$\mathbf{H} = \begin{pmatrix} p_1 & \frac{p_2}{M-p_1}q_1 & \cdots & \frac{p_d}{M-p_1}q_1 \\ \frac{p_1}{M-p_2}q_2 & p_2 & \cdots & \frac{p_d}{M-p_2}q_2 \\ \vdots & \vdots & \ddots & \vdots \\ \frac{p_1}{M-p_d}q_d & \frac{p_2}{M-p_d}q_d & \cdots & p_d \end{pmatrix},$$

where  $M = \sum_{j=1}^d p_j$ , and

$$v_i = \frac{p_i(M - p_i)/q_i}{\sum_{j=1}^d p_j(M - p_j)/q_j}, \quad i = 1, \dots, d.$$

The next example is an extension of Example 2.1.

**Example 2.2.** Let  $0 \leq \alpha < \infty$ . At the  $m$ th stage, if the response is a failure, we assign the  $(m + 1)$ th patient to treatment  $j$  with probability  $\frac{\hat{p}_{m-1,j}^\alpha}{(M_{m-1,\alpha} - \hat{p}_{m-1,k}^\alpha)}$  for all  $j \neq k$ , instead, where  $M_{m-1,\alpha} = \sum_{j=1}^d \hat{p}_{m-1,j}^\alpha$ . In this case,  $\mathbf{H}(\mathbf{x}) = (h_{k,j}(\mathbf{x}), k, j = 1, \dots, d)$ , where  $h_{k,k}(\mathbf{x}) = p_k$  and  $h_{k,j}(\mathbf{x}) = \frac{x_j^\alpha q_k}{\sum_{i \neq k} x_i^\alpha}$  for  $k \neq j$ . Also,

$$\mathbf{H} = \mathbf{H}^{(\alpha)} =: \begin{pmatrix} p_1 & \frac{p_2^\alpha}{M_\alpha - p_1^\alpha}q_1 & \cdots & \frac{p_d^\alpha}{M_\alpha - p_1^\alpha}q_1 \\ \frac{p_1^\alpha}{M_\alpha - p_2^\alpha}q_2 & p_2 & \cdots & \frac{p_d^\alpha}{M_\alpha - p_2^\alpha}q_2 \\ \vdots & \vdots & \ddots & \vdots \\ \frac{p_1^\alpha}{M_\alpha - p_d^\alpha}q_d & \frac{p_2^\alpha}{M_\alpha - p_d^\alpha}q_d & \cdots & p_d \end{pmatrix},$$

where  $M_\alpha = \sum_{j=1}^d p_j^\alpha$ , and

$$v_i = v_i^{(\alpha)} =: \frac{p_i^\alpha(M_\alpha - p_i^\alpha)/q_i}{\sum_{j=1}^d p_j^\alpha(M_\alpha - p_j^\alpha)/q_j}, \quad i = 1, \dots, d.$$

For these two examples, (2.4) holds. Example 2.1 is a special case of Example 2.2 with  $\alpha = 1$ . When  $\alpha = 0$ , then  $\mathbf{H}^{(\alpha)}$  and  $v_i^{(\alpha)}$  become

$$\mathbf{H}^{(0)} = \begin{pmatrix} p_1 & \frac{1}{d-1}q_1 & \cdots & \frac{1}{d-1}q_1 \\ \frac{1}{d-1}q_2 & p_2 & \cdots & \frac{1}{d-1}q_2 \\ \cdots & \cdots & \cdots & \cdots \\ \frac{1}{d-1}q_d & \frac{1}{d-1}q_d & \cdots & p_d \end{pmatrix},$$

and

$$v_i^{(0)} =: \frac{1/q_i}{\sum_{j=1}^d 1/q_j}, \quad i = 1, \dots, d.$$

By comparing the values of  $\mathbf{v}^{(\alpha)}$ 's, one can find the larger  $\alpha$ . Then more patients will be assigned to a better treatment. It is obvious that  $v_i^{(0)} = v_i^{\text{PWC}}, i = 1, \dots, d$ . Hence, the design in Examples 2.1 or 2.2 can assign more patients to better treatments than the PWC rule can. Also, when there is a failure, the assignment is random in the designs defined in these two examples. Hence, these designs are not so deterministic as the PWC rule.

**Remark 2.3.** When  $d = 2$ , the designs in Examples 2.1 and 2.2 are all PW rule.

**Remark 2.4.** Using the GPU model, Bai et al. [4] proposed a design similar to that in Examples 2.1. But for the GPU model, to study the asymptotic normality, we need a very stringent condition, that is,  $\max\{Re(\lambda_2), \dots, Re(\lambda_d)\} \leq 1/2$ . Even in the three-treatment case, such a condition is not easy to check.

Finally we give an example for the two-treatment case.

**Example 2.3.** We consider the two-treatment adaptive design. At the  $m$ th stage, no matter what the response of the  $m$ th patient is, we assign the  $(m + 1)$ th patient to treatment  $j$  with probability  $\frac{\hat{q}_{m-1,j}}{\hat{q}_{m-1,1} + \hat{q}_{m-1,2}}, j = 1, 2$ . This is the sequential maximum likelihood procedure proposed by Melfi and Page [9,10] and Melfi et al. [11]. If  $0 < p_1, p_2 < 1$ , then

$$\mathbf{H}(\mathbf{x}) = \begin{pmatrix} \frac{1-x_2}{(1-x_1)+(1-x_2)} & \frac{1-x_1}{(1-x_1)+(1-x_2)} \\ \frac{1-x_2}{(1-x_1)+(1-x_2)} & \frac{1-x_1}{(1-x_1)+(1-x_2)} \end{pmatrix} \rightarrow \mathbf{H} = \begin{pmatrix} \frac{q_2}{q_1+q_2} & \frac{q_1}{q_1+q_2} \\ \frac{q_2}{q_1+q_2} & \frac{q_1}{q_1+q_2} \end{pmatrix}.$$

We have the following asymptotic properties:

$$\begin{aligned} \frac{N_{n,1}}{n} - \frac{q_2}{q_1 + q_2} &= O\left(\sqrt{\frac{\log \log n}{n}}\right) \quad \text{and} \\ \frac{N_{n,2}}{n} - \frac{q_1}{q_1 + q_2} &= O\left(\sqrt{\frac{\log \log n}{n}}\right) \quad \text{a.s.} \end{aligned}$$

and

$$n^{1/2} \left( \frac{N_{n,1}}{n} - \frac{q_2}{q_1 + q_2}, \frac{N_{n,2}}{n} - \frac{q_1}{q_1 + q_2} \right) \xrightarrow{\mathcal{D}} N(0, \sigma^2)(1, -1),$$

where

$$\sigma^2 = \frac{q_1 q_2 (2 + p_1 + p_2)}{(q_1 + q_2)^3}. \quad (2.6)$$

This design gives the same limiting proportions as the PW rule does.

### 3. Asymptotic properties

To study the precise asymptotic properties, we first need some assumptions.

**Assumption 3.1.** For the matrix  $\mathbf{H}$  and the vector  $\mathbf{v}$ , we assume that  $\lambda < 1$  and  $v_i > 0$ ,  $i = 1, \dots, d$ .

This assumption is satisfied if  $\mathbf{H}$  is a regular transition matrix of a Markov chain, i.e., all of the elements of  $\mathbf{H}^q$  are strictly positive for some  $q = 1, 2, \dots$ . Then the assumption is satisfied for all the designs in Examples 2.1–2.3 since  $h_{ij} > 0$  for all  $i, j = 1, \dots, d$ .

**Assumption 3.2.** For the responses  $\xi_n$ , we assume that

$$E\|\xi_n\|^{2+\delta} \leq c_0 < \infty \quad \text{for some } \delta > 1$$

and write  $\sigma_k^2 = \text{Var}(\xi_{1,k})$ ,  $k = 1, \dots, d$ .

**Assumption 3.3.** For the matrix function  $\mathbf{H}(\mathbf{x})$ , we assume that

$$\mathbf{H}(\mathbf{x}) - \mathbf{H} = \mathbf{H}(\mathbf{x}) - \mathbf{H}(\boldsymbol{\theta}) = O(\|\mathbf{x} - \boldsymbol{\theta}\|) \quad \text{as } \mathbf{x} \rightarrow \boldsymbol{\theta}.$$

**Assumption 3.4.** For the matrix function  $\mathbf{H}(\mathbf{x})$ , we assume that for some  $\delta > 0$ ,

$$\mathbf{H}(\mathbf{x}) - \mathbf{H} = \sum_{k=1}^d \frac{\partial \mathbf{H}(\mathbf{x})}{\partial x_k} \bigg|_{\mathbf{x}=\boldsymbol{\theta}} (x_k - \theta_k) + O(\|\mathbf{x} - \boldsymbol{\theta}\|^{1+\delta}) \quad \text{as } \mathbf{x} \rightarrow \boldsymbol{\theta}.$$

Using the notation and assumptions defined as above, we can now establish the following results.

**Theorem 3.1.** For Adaptive Design 1, suppose  $E\|\xi_1\| < \infty$  and  $\lambda_j \neq 1$ ,  $j = 2, \dots, d$ . Then

$$\frac{\mathbf{N}_n}{n} \rightarrow \mathbf{v} \quad \text{a.s.}$$

**Theorem 3.2.** For Adaptive Design 1, under Assumptions 3.1–3.3,

$$\frac{\mathbf{N}_n}{n} - \mathbf{v} = O\left(\sqrt{\frac{\log \log n}{n}}\right) \quad \text{a.s.} \quad (3.1)$$

The next theorem gives us the strong approximation of  $\mathbf{N}_n$ .

**Theorem 3.3.** For the Adaptive Design 1, suppose Assumptions 3.1, 3.2 and 3.4 are satisfied. Define  $\tilde{\mathbf{H}} = \mathbf{H} - \mathbf{1}'\mathbf{v}$  and

$$\begin{aligned}\Sigma &= (\mathbf{I} - \tilde{\mathbf{H}}')^{-1}(\text{diag}(\mathbf{v}) - \mathbf{H}'\text{diag}(\mathbf{v})\mathbf{H})(\mathbf{I} - \tilde{\mathbf{H}})^{-1}, \\ \mathbf{f}_k &= \mathbf{v} \frac{\partial \mathbf{H}(\mathbf{x})}{\partial x_k} \Big|_{\mathbf{x}=\boldsymbol{\theta}}, \quad \mathbf{F} = (\mathbf{f}'_1, \dots, \mathbf{f}'_d)', \\ \mathbf{F}_{\dagger} &= \mathbf{F}(\mathbf{I} - \tilde{\mathbf{H}})^{-1}, \quad \Sigma_{\dagger} = \mathbf{F}'_{\dagger} \text{diag}(\sigma_1^2/v_1, \dots, \sigma_d^2/v_d) \mathbf{F}_{\dagger}.\end{aligned}\quad (3.2)$$

Then possibly in a richer underlying probability space in which there exist two independent  $d$ -dimensional standard Brownian motions  $\{\mathbf{B}_t\}$  and  $\{\mathbf{W}_t\}$ , we can redefine the sequence  $\{\mathbf{X}_n, \xi_n\}$  without changing its distribution, such that

$$\begin{aligned}\hat{\boldsymbol{\theta}}_n - \boldsymbol{\theta} &= \frac{1}{n} \mathbf{W}_n \text{diag}(\sigma_1/\sqrt{v_1}, \dots, \sigma_d/\sqrt{v_d}) + o(n^{1/2-\kappa}), \\ \mathbf{N}_n - n\mathbf{v} &= \mathbf{B}_n \Sigma^{1/2} + \int_0^n \frac{\mathbf{W}_t}{t} dt \Sigma_{\dagger}^{1/2} + o(n^{1/2-\kappa}) \quad a.s.,\end{aligned}\quad (3.3)$$

for some  $\kappa > 0$ . In particular,

$$n^{1/2} \left( \frac{\mathbf{N}_n}{n} - \mathbf{v}, \hat{\boldsymbol{\theta}}_n - \boldsymbol{\theta} \right) \xrightarrow{\mathcal{D}} N \left( \mathbf{0}, \begin{pmatrix} \Lambda & \mathbf{F}'_{\dagger} \Lambda_{\dagger} \\ \Lambda_{\dagger} \mathbf{F}_{\dagger} & \Lambda_{\dagger} \end{pmatrix} \right),$$

where

$$\Lambda = \Sigma + 2\Sigma_{\dagger} \quad \text{and} \quad \Lambda_{\dagger} = \text{diag}(\sigma_1^2/v_1, \dots, \sigma_d^2/v_d), \quad (3.4)$$

and also

$$n^{-1/2}(\mathbf{N}_{[nt]} - nt\mathbf{v}) \xrightarrow{\mathcal{D}} \mathbf{B}_t \Sigma^{1/2} + \int_0^t \frac{\mathbf{W}_s}{s} ds \Sigma_{\dagger}^{1/2}$$

in the space  $D[0, 1]$  with the Skorohod topology.

**Remark 3.1.** Notice that all eigenvalues of  $\tilde{\mathbf{H}}$  are 0,  $\lambda_2, \dots, \lambda_d$ , and the all eigenvalues of  $\mathbf{I} - \tilde{\mathbf{H}}$  are 1,  $1 - \lambda_2, \dots, 1 - \lambda_d$ . So, if  $\lambda_i \neq 1, i = 2, \dots, d$ , then  $(\mathbf{I} - \tilde{\mathbf{H}})^{-1}$  exists.

**Remark 3.2.** If the probabilities of assignments do not depend on the estimated parameters, i.e.,  $\mathbf{H}(\mathbf{x}) \equiv \mathbf{H}$ , then  $\Sigma_{\dagger} = \mathbf{0}$ . Hence, the second term in the right-hand side of (3.3) and (3.4) will not appear.

**Remark 3.3.** From the proof of Theorem 3.3, we may estimate  $\Lambda$  (the asymptotic covariance matrix of  $n^{-1/2}\mathbf{N}_n$ ) based on the following procedure:

- (i) Let  $\hat{v}_k = N_{n,k}/n, k = 1, \dots, d$ , and  $\hat{\mathbf{v}} = (\hat{v}_1, \dots, \hat{v}_d)$ . Estimate  $\mathbf{H}$  by  $\hat{\mathbf{H}} = \mathbf{H}(\hat{\boldsymbol{\theta}})$ , and  $\mathbf{f}_k$  by  $\hat{\mathbf{f}}_k = \mathbf{v} \frac{\partial \mathbf{H}(\mathbf{x})}{\partial x_k} \Big|_{\mathbf{x}=\hat{\boldsymbol{\theta}}}, k = 1, \dots, d$ . Write  $\hat{\mathbf{F}} = (\hat{\mathbf{f}}'_1, \dots, \hat{\mathbf{f}}'_d)'$ .
- (ii) Let  $\hat{\sigma}_k^2 = \sum_{i=1}^n X_{i,k}(\xi_{i,k} - \hat{\theta}_k)^2 / N_{n,k}$  be the estimators of  $\sigma_k^2$ , for  $k = 1, \dots, d$ . And let  $\hat{\Lambda}_{\dagger} = \text{diag}(\hat{\sigma}_1^2/\hat{v}_1, \dots, \hat{\sigma}_d^2/\hat{v}_d)$  be the estimator of  $\Lambda_{\dagger}$ .



(iii) Let  $\widehat{\widehat{\mathbf{H}}} = \widehat{\mathbf{H}} - \mathbf{1}'\widehat{\mathbf{v}}$  and use

$$\widehat{\mathbf{\Lambda}} = [(\mathbf{I} - \widehat{\widehat{\mathbf{H}}})^{-1}]' [\text{diag}(\widehat{\mathbf{v}}) - \widehat{\mathbf{H}}' \text{diag}(\widehat{\mathbf{v}}) \widehat{\mathbf{H}} + 2\widehat{\mathbf{F}}' \widehat{\mathbf{\Lambda}}_{\dagger} \widehat{\mathbf{F}}] (\mathbf{I} - \widehat{\widehat{\mathbf{H}}})^{-1}$$

to estimate  $\mathbf{\Lambda}$ . Based on  $\widehat{\mathbf{\Lambda}}$ , we can assess the variation of designs.

**Remark 3.4.** If the responses  $\xi_n$ ,  $n \geq 1$ , are not identically distributed, then under the conditions in Theorems 3.1–3.3, we have, respectively,

$$\mathbf{N}_n - n\mathbf{v} = O\left(\sum_{m=1}^n \|E\xi_m - \theta\|\right) \quad \text{a.s.},$$

$$\mathbf{N}_n - n\mathbf{v} = O\left(\sqrt{n \log \log n}\right) + O\left(\sum_{m=1}^n \|E\xi_m - \theta\|\right) \quad \text{a.s.},$$

$$\begin{aligned} \mathbf{N}_n - n\mathbf{v} &= \mathbf{B}_n \mathbf{\Sigma}^{1/2} + \int_0^n \frac{\mathbf{W}_t}{t} dt \mathbf{\Sigma}_{\dagger}^{1/2} + o(n^{1/2-\kappa}) \\ &\quad + O\left(\sum_{m=1}^n \|E\xi_m - \theta\|\right) + O\left(\left\{\sum_{m=1}^n \sum_{i=1}^d |\text{Var}(\xi_{m,i}) - \sigma_i^2|\right\}^{1/2+\delta}\right) \quad \text{a.s.} \end{aligned}$$

#### 4. Proofs

We start with some lemmas that will be used to prove the strong consistency and its convergence rate.

**Lemma 4.1.** *If  $E\|\xi_1\| < \infty$ , then  $\widehat{\theta}_{n,k} \rightarrow \theta_k$  a.s. as  $n \rightarrow \infty$  on the event  $\{N_{n,k} \rightarrow \infty\}$ ,  $k = 1, \dots, d$ . Furthermore, if  $E\|\xi_1\|^2 < \infty$ , then  $\widehat{\theta}_{n,k} - \theta_k = O\left(\sqrt{\frac{\log \log N_{n,k}}{N_{n,k}}}\right)$  a.s. as  $n \rightarrow \infty$  on the event  $\{N_{n,k} \rightarrow \infty\}$ ,  $k = 1, \dots, d$ .*

**Proof.** For  $k = 1, \dots, d$ , define  $\tau_i^k = \min\{j : N_{j,k} = i\}$ , where  $\min\{\emptyset\} = +\infty$ . Let  $\{\eta_{i,k}\}$  be an independent copy of  $\{\xi_{i,k}\}$ , which is also independent of  $\{\mathbf{X}_i\}$ . Define  $\Xi_{i,k} = \xi_{\tau_i^k, k} I\{\tau_i^k < +\infty\} + \eta_{i,k} I\{\tau_i^k = +\infty\}$ ,  $i \geq 1$ . Then,  $\{\Xi_{m,k}, m = 1, 2, \dots\}$  is a sequence of i.i.d. random variables, with the same distribution as that of  $\xi_{1,k}$  (cf., [4]). Also,  $\widehat{\theta}_{n,k} = \frac{1}{N_{n,k}+1} (\sum_{i=1}^{N_{n,k}} \Xi_{m,k} + 1)$  on the event  $\{N_{n,k} \rightarrow \infty\}$ . The results follow by the law of large numbers and the law of the iterated logarithm for sums of i.i.d. random variables.  $\square$

**Lemma 4.2.** *For Adaptive Design 1, we have*

$$N_{n,k} \rightarrow \infty \quad \text{a.s.}, \quad k = 1, \dots, d.$$

**Proof.** For each fixed  $k$ , it is obvious that

$$\sum_{m=2}^{\infty} P(X_{m+1,k} = 1 | \mathcal{F}_m) \geq \sum_{m=2}^{\infty} \frac{1}{md} = +\infty \quad \text{a.s.},$$

which implies that  $P(X_{m,k} = 1, \text{i.o.}) = 1$  by the generalized Borel–Cantelli lemma (cf., [5]). It follows that  $N_{n,k} \rightarrow \infty$  a.s. If (2.2) is satisfied, then the proof is similar.  $\square$

**Proof of Theorem 3.1.** Write

$$h_{ij}(m) = \left(1 - \frac{1}{m}\right) h_{ij}(\hat{\theta}_{m-1}) + \frac{1}{md} \quad \text{and} \quad \mathbf{H}_m = (h_{ij}(m))_{i,j=1}^d.$$

From (2.1), it follows that

$$P(X_{m+1,j} = 1 | \mathcal{F}_m, X_{m,i} = 1) = h_{ij}(m), \quad i, j = 1, \dots, d,$$

i.e.,

$$P(\mathbf{X}_{m+1} = \mathbf{e}_j | \mathbf{X}_m = \mathbf{e}_i, \mathcal{F}_m) = h_{ij}(m),$$

where  $\mathbf{e}_i$  is a vector whose  $i$ th component is 1 and other components are 0,  $i = 1, \dots, d$ . It follows that:

$$E[\mathbf{X}_{m+1} | \mathcal{F}_m] = \mathbf{X}_m \mathbf{H}_m. \quad (4.1)$$

So,  $\{\mathbf{X}_m\}$  looks like a non-homogeneous Markov chain with transition matrix  $\mathbf{H}_n$ .

Let  $\mathbf{Z}_n = \mathbf{X}_n - E[\mathbf{X}_n | \mathcal{F}_{n-1}]$ , and  $\mathbf{M}_n = \sum_{k=1}^n \mathbf{Z}_k$ . By (4.1), it is easily seen that

$$\begin{aligned} \mathbf{X}_n &= \mathbf{Z}_n + \mathbf{X}_{n-1} \mathbf{H}_{n-1} = \mathbf{Z}_n + (\mathbf{X}_{n-1} - \mathbf{v}) \mathbf{H} + \mathbf{v} + \mathbf{X}_{n-1} (\mathbf{H}_{n-1} - \mathbf{H}) \\ &= \mathbf{Z}_n + (\mathbf{X}_{n-1} - \mathbf{v}) \tilde{\mathbf{H}} + \mathbf{v} + \mathbf{X}_{n-1} (\mathbf{H}_{n-1} - \mathbf{H}) \end{aligned}$$

since  $\mathbf{vH} = \mathbf{v}$  and  $(\mathbf{X}_{n-1} - \mathbf{v})\mathbf{1}' = 1 - 1 = 0$ . So,

$$\sum_{k=1}^n (\mathbf{X}_k - \mathbf{v}) = \mathbf{M}_n + \sum_{k=1}^n (\mathbf{X}_k - \mathbf{v}) \tilde{\mathbf{H}} + \sum_{k=1}^n \mathbf{X}_k (\mathbf{H}_k - \mathbf{H}) + E[\mathbf{X}_1 | \mathcal{F}_0] - E[\mathbf{X}_{n+1} | \mathcal{F}_n].$$

It follows that

$$(\mathbf{N}_n - n\mathbf{v})(\mathbf{I} - \tilde{\mathbf{H}}) = \mathbf{M}_n + \sum_{k=1}^n \mathbf{X}_k (\mathbf{H}_k - \mathbf{H}) + E[\mathbf{X}_1] - E[\mathbf{X}_{n+1} | \mathcal{F}_n]. \quad (4.2)$$

On the other hand, it is obvious that  $\|\mathbf{Z}_n\| \leq 2$ . By the law of the iterated logarithm for martingales (cf., [15, Theorem 5.4.1]), one has

$$\mathbf{M}_n = O\left(\sqrt{n \log \log n}\right) \quad \text{a.s.} \quad (4.3)$$

Now, by Lemmas 4.1 and 4.2, we have  $\hat{\theta}_n \rightarrow \theta$  a.s. as  $n \rightarrow \infty$ . So,  $\mathbf{H}(\hat{\theta}_n) \rightarrow \mathbf{H}(\theta)$  a.s.  $n \rightarrow \infty$ . It follows that  $\mathbf{H}_n \rightarrow \mathbf{H}$ . Hence,

$$\sum_{k=1}^n \|\mathbf{H}_k - \mathbf{H}\| = o(n) \quad \text{a.s.},$$

which together with (4.2) and (4.3) implies  $(\mathbf{N}_n - n\mathbf{v})(\mathbf{I} - \tilde{\mathbf{H}}) = o(n)$  a.s. Notice that  $(\mathbf{I} - \tilde{\mathbf{H}})^{-1}$  exists under the condition that  $\lambda_j \neq \lambda_1 = 1$  for  $j \neq 1$ . The proof is now completed.  $\square$

**Proof of Theorem 3.2.** From Theorem 3.1, it follows that

$$\frac{1}{N_{n,k}} \sim \frac{1}{nv_k} \quad \text{a.s. } (n \rightarrow \infty), \quad k = 1, \dots, d.$$

So, by Lemmas 4.1 and 4.2,

$$\hat{\theta}_{n,k} - \theta_k = O\left(\sqrt{\frac{\log \log N_{n,k}}{N_{n,k}}}\right) = O\left(\sqrt{\frac{\log \log n}{n}}\right) \quad \text{a.s. } k = 1, \dots, d.$$

Thus,

$$\hat{\theta}_n - \theta = O\left(\sqrt{\frac{\log \log n}{n}}\right) \quad \text{a.s.,} \quad (4.4)$$

which, together with Assumption 3.4, implies that

$$\mathbf{H}_n - \mathbf{H} = \mathbf{H}(\hat{\theta}_{n-1}) - \mathbf{H}(\theta) + O\left(\frac{1}{n}\right) = O\left(\sqrt{\frac{\log \log n}{n}}\right) \quad \text{a.s.} \quad (4.5)$$

Hence,

$$\sum_{k=1}^n \|\mathbf{H}_k - \mathbf{H}\| = \sum_{k=1}^n O\left(\sqrt{\frac{\log \log k}{k}}\right) = O\left(\sqrt{n \log \log n}\right) \quad \text{a.s.}$$

By combining (4.2), (4.3) and the above equation, we conclude that  $(\mathbf{N}_n - n\mathbf{v})(\mathbf{I} - \tilde{\mathbf{H}}) = O(\sqrt{n \log \log n})$  a.s. The proof is now completed.  $\square$

**Proof of (2.2) in Remark 2.1.** By Lemma 4.1,  $\hat{\theta}_{m,j} \rightarrow \theta_j$  a.s. on the event  $\{N_{m,j} \rightarrow \infty\}$ . Also, on the event  $\{\sup_m N_{m,j} < \infty\}$ , there exists a positive number  $m_0$ , such that,  $\hat{\theta}_{m,j} = \hat{\theta}_{m_0,j}$  for all  $m \geq m_0$ . It follows that

$$\text{the closure of } \{\hat{\theta}_m; m = 1, 2, \dots\} \subset \{\mathbf{x} : h_{ij}(\mathbf{x}) > 0, i, j = 1, \dots, d\} \quad \text{a.s.}$$

So, by the continuity of  $\mathbf{H}(x)$ , with probability 1 there is an  $c_0 > 0$  such that

$$h_{ij}(\hat{\theta}_m) \geq c_0 \quad \text{for all } i, j = 1, \dots, d \text{ and } m \geq 1.$$

(2.2) is proved.  $\square$

Now, we begin the proof of Theorem 3.3. Recall (4.2), in which the martingale  $\mathbf{M}_n$  can be approximated by a Wiener process. If the term  $\sum_{k=1}^n \mathbf{X}_k(\mathbf{H}_k - \mathbf{H})$  is asymptotically negligible, the Gaussian approximation of  $\mathbf{N}_n$  can be gotten easily. However, by (4.5), the fastest convergence rate of  $\sum_{k=1}^n \mathbf{X}_k(\mathbf{H}_k - \mathbf{H})$  is  $O(\sqrt{n \log \log n})$ . So we shall do something

else to deal with this term. At first, we will give the other three lemmas. The first one shows that  $\sum_{k=1}^n \mathbf{X}_k(\mathbf{H}_k - \mathbf{H})$  can be approximated by  $\sum_{k=1}^n \mathbf{v}(\mathbf{H}_k - \mathbf{H})$ .

**Lemma 4.3.** *If  $\lambda = \max\{|\lambda_2|, \dots, |\lambda_d|\} < 1$ , then*

$$\begin{aligned} & \left\| \sum_{k=1}^n \mathbf{X}_k(\mathbf{H}_k - \mathbf{H}) - \sum_{k=1}^n \mathbf{v}(\mathbf{H}_k - \mathbf{H}) \right\| \\ & \leq C + C \left\| \sum_{k=2}^n \mathbf{Z}_k(\mathbf{I} - \tilde{\mathbf{H}})^{-1}(\mathbf{H}_{k-1} - \mathbf{H}) \right\| \\ & \quad + C \sum_{k=2}^n \|\mathbf{H}_k - \mathbf{H}_{k-1}\| + C \sum_{k=1}^n \|\mathbf{H}_k - \mathbf{H}\|^2. \end{aligned} \quad (4.6)$$

**Proof.** Without loss of generality, we can assume that  $\|\mathbf{x}\|$  is the Euclidean norm of  $\mathbf{x}$ ,  $\forall \mathbf{x} \in \mathbb{R}^d$ , and  $\|\mathbf{M}\| = \sup_{\mathbf{x} \neq \mathbf{0}} \|\mathbf{xM}\|/\|\mathbf{x}\|$  is the norm of a  $d \times d$  matrix  $\mathbf{M}$ . Write  $\mathbf{H}_0 = \mathbf{e}_1' \mathbf{E} \mathbf{X}_1$ . For  $k \leq 0$ , let  $\mathbf{X}_k = \mathbf{E} \mathbf{X}_1$ ,  $\mathbf{H}_k = \mathbf{H}_0$ ,  $\mathcal{F}_k = \mathcal{F}_0$  and  $\mathbf{Z}_k = \mathbf{0}$ . Then, for  $p \geq n \geq 1$ ,

$$\begin{aligned} \sum_{k=1}^n \mathbf{X}_k(\mathbf{H}_k - \mathbf{H}) &= \sum_{k=1}^n \mathbf{Z}_k(\mathbf{H}_k - \mathbf{H}) + \sum_{k=1}^n \mathbf{X}_{k-1} \mathbf{H}_{k-1}(\mathbf{H}_k - \mathbf{H}) \\ &= \sum_{k=1}^n \mathbf{Z}_k(\mathbf{H}_k - \mathbf{H}) + \sum_{k=1}^n \mathbf{X}_{k-1} \mathbf{H}(\mathbf{H}_k - \mathbf{H}) \\ & \quad + \sum_{k=1}^n \mathbf{X}_{k-1}(\mathbf{H}_{k-1} - \mathbf{H})(\mathbf{H}_k - \mathbf{H}) \\ &= \sum_{k=1}^n \mathbf{Z}_k(\mathbf{H}_k - \mathbf{H}) + \sum_{k=1}^n \mathbf{Z}_{k-1} \mathbf{H}(\mathbf{H}_k - \mathbf{H}) + \sum_{k=1}^n \mathbf{X}_{k-2} \mathbf{H}^2(\mathbf{H}_k - \mathbf{H}) \\ & \quad + \sum_{k=1}^n \mathbf{X}_{k-1}(\mathbf{H}_{k-1} - \mathbf{H})(\mathbf{H}_k - \mathbf{H}) + \sum_{k=1}^n \mathbf{X}_{k-2}(\mathbf{H}_{k-2} - \mathbf{H})\mathbf{H}(\mathbf{H}_k - \mathbf{H}) \\ &= \dots = \sum_{k=1}^n \sum_{j=0}^p \mathbf{Z}_{k-j} \mathbf{H}^j(\mathbf{H}_k - \mathbf{H}) + \sum_{k=1}^n \mathbf{X}_{k-p} \mathbf{H}^p(\mathbf{H}_k - \mathbf{H}) \\ & \quad + \sum_{k=1}^n \sum_{j=1}^p \mathbf{X}_{k-j}(\mathbf{H}_{k-j} - \mathbf{H})\mathbf{H}^{j-1}(\mathbf{H}_k - \mathbf{H}). \end{aligned}$$

Observe that  $\mathbf{X}_j \mathbf{1}' = 1$ ,  $\mathbf{Z}_j \mathbf{1}' = 0$ ,  $\mathbf{H}^j - \mathbf{1}' \mathbf{v} = (\mathbf{H} - \mathbf{1}' \mathbf{v})^j = \tilde{\mathbf{H}}^j$  and  $(\mathbf{H}_j - \mathbf{H}) \mathbf{1}' = \mathbf{1}' - \mathbf{1}' = \mathbf{0}$ . We have

$$\begin{aligned} \mathbf{X}_{k-p} \mathbf{H}^p(\mathbf{H}_k - \mathbf{H}) &= \mathbf{X}_{k-p}(\mathbf{H}^p - \mathbf{1}' \mathbf{v})(\mathbf{H}_k - \mathbf{H}) + \mathbf{X}_{k-p} \mathbf{1}' \mathbf{v}(\mathbf{H}_k - \mathbf{H}) \\ &= \mathbf{X}_{k-p} \tilde{\mathbf{H}}^p(\mathbf{H}_k - \mathbf{H}) + \mathbf{v}(\mathbf{H}_k - \mathbf{H}), \end{aligned}$$

$$\mathbf{Z}_{k-j} \mathbf{H}^j(\mathbf{H}_k - \mathbf{H}) = \mathbf{Z}_{k-j} \tilde{\mathbf{H}}^j(\mathbf{H}_k - \mathbf{H})$$

and

$$\mathbf{X}_{k-j}(\mathbf{H}_{k-j} - \mathbf{H})\mathbf{H}^{j-1}(\mathbf{H}_k - \mathbf{H}) = \mathbf{X}_{k-j}(\mathbf{H}_{k-j} - \mathbf{H})\tilde{\mathbf{H}}^{j-1}(\mathbf{H}_k - \mathbf{H}).$$

We conclude that

$$\begin{aligned} & \sum_{k=1}^n \mathbf{X}_k(\mathbf{H}_k - \mathbf{H}) \\ &= \sum_{k=1}^n \mathbf{v}(\mathbf{H}_k - \mathbf{H}) + \sum_{k=1}^n \sum_{j=0}^p \mathbf{Z}_{k-j} \tilde{\mathbf{H}}^j (\mathbf{H}_k - \mathbf{H}) \\ & \quad + \sum_{k=1}^n \sum_{j=1}^p \mathbf{X}_{k-j}(\mathbf{H}_{k-j} - \mathbf{H}) \tilde{\mathbf{H}}^{j-1}(\mathbf{H}_k - \mathbf{H}) + \sum_{k=1}^n \mathbf{X}_{k-p} \tilde{\mathbf{H}}^p (\mathbf{H}_k - \mathbf{H}) \\ &= \sum_{k=1}^n \mathbf{v}(\mathbf{H}_k - \mathbf{H}) + \sum_{k=1}^n \sum_{j=0}^p \mathbf{Z}_{k-j} \tilde{\mathbf{H}}^j (\mathbf{H}_{k-j-1} - \mathbf{H}) + \sum_{k=1}^n \sum_{j=0}^p \mathbf{Z}_{k-j} \tilde{\mathbf{H}}^j (\mathbf{H}_k - \mathbf{H}_{k-j-1}) \\ & \quad + \sum_{k=1}^n \sum_{j=1}^p \mathbf{X}_{k-j}(\mathbf{H}_{k-j} - \mathbf{H}) \tilde{\mathbf{H}}^{j-1}(\mathbf{H}_k - \mathbf{H}) + \sum_{k=1}^n \mathbf{X}_{k-p} \tilde{\mathbf{H}}^p (\mathbf{H}_k - \mathbf{H}) \\ &=: \sum_{k=1}^n \mathbf{v}(\mathbf{H}_k - \mathbf{H}) + I_1 + I_2 + I_3 + I_4. \end{aligned} \quad (4.7)$$

Notice that  $\lim_{j \rightarrow \infty} \|\tilde{\mathbf{H}}^j\|^{1/j} = |\lambda| < 1$ . So, for  $|\lambda| < \rho < 1$ , there exists a constant  $C > 0$  such that  $\|\tilde{\mathbf{H}}^j\| \leq C\rho^j$ ,  $j \geq 0$ . It follows that

$$\begin{aligned} \|I_1\| &= \left\| \sum_{k=1}^n \sum_{j=0}^p \mathbf{Z}_{k-j} \tilde{\mathbf{H}}^j (\mathbf{H}_{k-j-1} - \mathbf{H}) \right\| = \left\| \sum_{j=0}^p \sum_{k=j}^n \mathbf{Z}_{k-j} \tilde{\mathbf{H}}^j (\mathbf{H}_{k-j-1} - \mathbf{H}) \right\| \\ &= \left\| \sum_{j=0}^p \sum_{l=0}^{n-j} \mathbf{Z}_l \tilde{\mathbf{H}}^j (\mathbf{H}_{l-1} - \mathbf{H}) \right\| = \left\| \sum_{l=0}^n \sum_{j=0}^{n-l} \mathbf{Z}_l \tilde{\mathbf{H}}^j (\mathbf{H}_{l-1} - \mathbf{H}) \right\| \\ &= \left\| \sum_{l=0}^n \sum_{j=0}^{\infty} \mathbf{Z}_l \tilde{\mathbf{H}}^j (\mathbf{H}_{l-1} - \mathbf{H}) - \sum_{l=0}^n \sum_{j=n-l}^{\infty} \mathbf{Z}_l \tilde{\mathbf{H}}^j (\mathbf{H}_{l-1} - \mathbf{H}) \right\| \\ &\leq \left\| \sum_{l=0}^n \mathbf{Z}_l (\mathbf{I} - \tilde{\mathbf{H}})^{-1} (\mathbf{H}_{l-1} - \mathbf{H}) \right\| + C \sum_{l=0}^n \sum_{j=n-l}^{\infty} \rho^j \|\mathbf{H}_{l-1} - \mathbf{H}\| \\ &\leq \left\| \sum_{l=1}^n \mathbf{Z}_l (\mathbf{I} - \tilde{\mathbf{H}})^{-1} (\mathbf{H}_{l-1} - \mathbf{H}) \right\| + C/(1 - \rho)^2, \end{aligned} \quad (4.8)$$

$$\|I_2\| \leq C \sum_{k=1}^n \sum_{j=0}^p \rho^j \|\mathbf{H}_k - \mathbf{H}_{k-j-1}\| \leq C \sum_{k=1}^n \sum_{j=0}^p \rho^j \sum_{i=0}^j \|\mathbf{H}_{k-i} - \mathbf{H}_{k-i-1}\|$$

$$\begin{aligned}
&\leq C \sum_{k=1}^n \sum_{i=0}^p \sum_{j=i}^p \rho^j \|\mathbf{H}_{k-i} - \mathbf{H}_{k-i-1}\| \leq C \sum_{k=1}^n \sum_{i=0}^p \rho^i \|\mathbf{H}_{k-i} - \mathbf{H}_{k-i-1}\| \\
&\leq C \sum_{i=0}^p \rho^i \sum_{k=1}^n \|\mathbf{H}_{k-i} - \mathbf{H}_{k-i-1}\| \leq C \sum_{i=0}^p \rho^i \sum_{k=1}^n \|\mathbf{H}_k - \mathbf{H}_{k-1}\| \\
&\leq C \sum_{k=1}^n \|\mathbf{H}_k - \mathbf{H}_{k-1}\|, \tag{4.10}
\end{aligned}$$

$$\begin{aligned}
\|I_3\| &\leq C \sum_{k=1}^n \sum_{j=1}^p \|\mathbf{H}_{k-j} - \mathbf{H}\| \cdot \rho^{j-1} \cdot \|\mathbf{H}_k - \mathbf{H}\| \\
&= C \sum_{j=1}^p \rho^{j-1} \sum_{k=1}^n \|\mathbf{H}_{k-j} - \mathbf{H}\| \cdot \|\mathbf{H}_k - \mathbf{H}\| \\
&\leq C \sum_{j=1}^p \rho^{j-1} \left( \sum_{k=1}^n \|\mathbf{H}_{k-j} - \mathbf{H}\|^2 \right)^{1/2} \left( \sum_{k=1}^n \|\mathbf{H}_k - \mathbf{H}\|^2 \right)^{1/2} \\
&\leq C \sum_{j=1}^p \rho^{j-1} \sum_{k=1-j}^n \|\mathbf{H}_k - \mathbf{H}\|^2 \\
&= C \sum_{j=1}^p j \rho^{j-1} \|\mathbf{H}_0 - \mathbf{H}\|^2 + C \sum_{j=1}^p \rho^{j-1} \sum_{k=1}^n \|\mathbf{H}_k - \mathbf{H}\|^2 \\
&\leq C \|\mathbf{H}_0 - \mathbf{H}\|^2 + C \sum_{k=1}^n \|\mathbf{H}_k - \mathbf{H}\|^2 \tag{4.11}
\end{aligned}$$

and

$$\|I_4\| \leq C \rho^p \sum_{k=1}^n \|\mathbf{H}_k - \mathbf{H}\|. \tag{4.12}$$

Substituting (4.9)–(4.12) into (4.7) and letting  $p \rightarrow \infty$  yields (4.6).  $\square$

The next two lemmas are related to the strong approximation for a martingale.

**Lemma 4.4.** Let  $\{\mathbf{S}_n = \sum_{k=1}^n \Delta \mathbf{S}_k, \mathcal{F}_n; n \geq 1\}$  be a sequence of  $\mathbb{R}^K$ -valued martingale, and let

$$T_n = \sum_{k=1}^n E[(\Delta \mathbf{S}_k)'(\Delta \mathbf{S}_k) | \mathcal{F}_{k-1}].$$

Suppose that there exists a constant  $0 < \varepsilon < 1$  such that

$$\sup_n E \|\Delta \mathbf{S}_n\|^{2+\varepsilon} < \infty. \tag{4.13}$$

Furthermore, suppose  $\mathbf{T}$  is a covariance matrix measurable with respect to  $\mathcal{F}_k$  for some  $k \geq 0$ . Then for any  $\delta > 0$ , possibly in a richer underlying probability space in which there exists a  $K$ -dimensional standard Brownian  $\{\mathbf{B}_t\}$ , we can redefine the sequence  $\{\mathbf{S}_n\}$  and  $\mathbf{T}$ , without changing their distributions, such that  $\{\mathbf{B}_t\}$  is independent of  $\mathbf{T}$ , and

$$\mathbf{S}_n - \mathbf{B}_n \mathbf{T}^{1/2} = O(n^{1/2-\kappa}) + O(\alpha_n^{1/2+\delta}) \text{ a.s.}$$

for some  $\kappa > 0$ . Here  $\alpha_n = \max_{m \leq n} \|\mathbf{T}_m - m\mathbf{T}\|$ .

**Proof.** This lemma is proved by [19], we omit the details here.  $\square$

**Lemma 4.5.** Denote  $\Sigma_1 = \text{diag}(\mathbf{v}) - \mathbf{H}' \text{diag}(\mathbf{v})\mathbf{H}$ . Let  $\mathbf{Q}_n = (Q_{n,1}, \dots, Q_{n,d}) = \sum_{k=1}^n \mathbf{q}_k$ , where  $\mathbf{q}_k = \mathbf{X}_k \text{diag}(\xi_k - \theta)$ . Suppose that Assumption 3.2 is satisfied. Then for any  $\delta > 0$ , there are two independent  $d$ -dimensional standard Brownian motions  $\mathbf{B}_t$  and  $\mathbf{W}_t$  and a positive number  $\kappa > 0$ , such that

$$\mathbf{M}_n - \mathbf{B}_n \Sigma_1^{1/2} = o(n^{1/2-\kappa}) + O\left(\left(\sum_{k=1}^n \|\mathbf{H}_n - \mathbf{H}\|\right)^{1/2+\delta}\right) \text{ a.s.},$$

$$\begin{aligned} \mathbf{Q}_n - \mathbf{W}_n \text{diag}(\sigma_1 \sqrt{v_1}, \dots, \sigma_d \sqrt{v_d}) &= o(n^{1/2-\kappa}) \\ &+ O\left(\left(\sum_{k=1}^n \|\mathbf{H}_n - \mathbf{H}\|\right)^{1/2+\delta}\right) \text{ a.s.} \end{aligned}$$

**Proof.** It is obvious that

$$\mathbb{E}[\mathbf{Z}'_n \mathbf{q}_n | \mathcal{F}_{n-1}] = \mathbb{E}[\mathbf{Z}'_n \mathbf{X}_n | \mathcal{F}_{n-1}] \text{diag}(\mathbb{E}[\xi_n - \theta]) = \mathbf{0} \quad (4.14)$$

and

$$\begin{aligned} \sum_{k=2}^n \mathbb{E}[\mathbf{q}'_k \mathbf{q}_k | \mathcal{F}_{k-1}] &= \sum_{k=2}^n \text{diag}(\sigma_1^2, \dots, \sigma_d^2) \text{diag}(\mathbf{X}_{k-1} \mathbf{H}_{k-1}) \\ &= \text{diag}(\sigma_1^2, \dots, \sigma_d^2) \text{diag}\left(\sum_{k=1}^{n-1} \mathbf{X}_k \mathbf{H}\right) \\ &\quad + \text{diag}(\sigma_1^2, \dots, \sigma_d^2) \text{diag}\left(\sum_{k=1}^{n-1} \mathbf{X}_k (\mathbf{H}_k - \mathbf{H})\right) \\ &= (n-1) \text{diag}(\sigma_1^2, \dots, \sigma_d^2) \text{diag}(\mathbf{v} \mathbf{H}) \\ &\quad + \text{diag}(\sigma_1^2, \dots, \sigma_d^2) \text{diag}((\mathbf{N}_{n-1} - (n-1)\mathbf{v}) \mathbf{H}) \\ &\quad + \text{diag}(\sigma_1^2, \dots, \sigma_d^2) \text{diag}\left(\sum_{k=1}^{n-1} \mathbf{X}_k (\mathbf{H}_k - \mathbf{H})\right). \end{aligned}$$

It follows that

$$\begin{aligned}
 & \left\| \sum_{k=1}^n E[\mathbf{q}'_n \mathbf{q}_n | \mathcal{F}_{n-1}] - n \operatorname{diag}(\sigma_1^2 v_1, \dots, \sigma_d^2 v_d) \right\| \\
 & \leq C + C \|\mathbf{N}_n - n\mathbf{v}\| + C \sum_{k=1}^n \|\mathbf{H}_k - \mathbf{H}\| \\
 & \leq C \sqrt{n \log \log n} + C \sum_{k=1}^n \|\mathbf{H}_k - \mathbf{H}\| \quad \text{a.s.}, \tag{4.15}
 \end{aligned}$$

by (4.2) and (4.3).

On the other hand, we can verify that

$$\begin{aligned}
 E[\mathbf{Z}'_n \mathbf{Z}_n | \mathcal{F}_{n-1}] &= E[\mathbf{X}'_n \mathbf{X}_n | \mathcal{F}_{n-1}] - (E[\mathbf{X}_n | \mathcal{F}_{n-1}])' E[\mathbf{X}_n | \mathcal{F}_{n-1}] \\
 &= \operatorname{diag}(\mathbf{X}_{n-1} \mathbf{H}_{n-1}) - \mathbf{H}'_{n-1} \operatorname{diag}(\mathbf{X}_{n-1}) \mathbf{H}_{n-1} \\
 &= \operatorname{diag}(\mathbf{v} \mathbf{H}) - \mathbf{H}' \operatorname{diag}(\mathbf{v}) \mathbf{H} - \mathbf{H}' \operatorname{diag}(\mathbf{X}_{n-1} - \mathbf{v}) \mathbf{H} + \operatorname{diag}[(\mathbf{X}_{n-1} - \mathbf{v}) \mathbf{H}] \\
 &\quad + \operatorname{diag}[\mathbf{X}_{n-1} (\mathbf{H}_{n-1} - \mathbf{H})] - \mathbf{H}'_{n-1} \operatorname{diag}(\mathbf{X}_{n-1}) (\mathbf{H}_{n-1} - \mathbf{H}) \\
 &\quad - (\mathbf{H}_{n-1} - \mathbf{H})' \operatorname{diag}(\mathbf{X}_{n-1}) \mathbf{H}.
 \end{aligned}$$

It follows that

$$\begin{aligned}
 & \left\| \sum_{k=1}^n E[\mathbf{Z}'_k \mathbf{Z}_k | \mathcal{F}_{k-1}] - n \boldsymbol{\Sigma}_1 \right\| \\
 & \leq \|\mathbf{H}' \operatorname{diag}(\mathbf{N}_{n-1} - n\mathbf{v}) \mathbf{H}\| + \|\operatorname{diag}[(\mathbf{N}_{n-1} - n\mathbf{v}) \mathbf{H}]\| + C \sum_{k=1}^n \|\mathbf{H}_n - \mathbf{H}\| + C \\
 & \leq C \|\mathbf{N}_n - n\mathbf{v}\| + C \sum_{k=1}^n \|\mathbf{H}_n - \mathbf{H}\| + C \tag{4.16}
 \end{aligned}$$

$$\leq C \left( \sqrt{n \log \log n} \right) + C \sum_{k=1}^n \|\mathbf{H}_n - \mathbf{H}\| \tag{4.17}$$

by (4.2) and (4.3) again. By (4.16), (4.14) and (4.15), applying Lemma 4.4 to the martingale sequence  $\{\sum_{k=1}^n (\mathbf{Z}_k, \mathbf{q}_k); n \geq 1\}$ , we complete the proof of Lemma 4.5.  $\square$

**Proof of Theorem 3.3.** Recall (4.2). First we apply Lemma 4.3 to show that

$$\sum_{k=1}^n \mathbf{X}_k (\mathbf{H}_k - \mathbf{H}) = \sum_{k=1}^n \frac{1}{k} \mathbf{Q}_k \operatorname{diag}(1/v_1, \dots, 1/v_d) \mathbf{F} + o(n^{1/2-\delta/3}) \quad \text{a.s.} \tag{4.18}$$

By Assumption 3.4 and (4.4),

$$\mathbf{H}_{n+1} - \mathbf{H} = \mathbf{H}(\hat{\boldsymbol{\theta}}_n) - \mathbf{H}(\boldsymbol{\theta}) + O\left(\frac{1}{n}\right)$$



$$\begin{aligned}
&= \sum_{k=1}^d \frac{\partial \mathbf{H}(\mathbf{x})}{\partial x_k} \Big|_{\mathbf{x}=\boldsymbol{\theta}} (\hat{\theta}_{n,k} - \theta_k) + O(\|\hat{\boldsymbol{\theta}}_n - \boldsymbol{\theta}\|^{1+\delta}) + O\left(\frac{1}{n}\right) \\
&= \sum_{k=1}^d \frac{\partial \mathbf{H}(\mathbf{x})}{\partial x_k} \Big|_{\mathbf{x}=\boldsymbol{\theta}} (\hat{\theta}_{n,k} - \theta_k) + o(n^{-1/2-\delta/3}) \quad \text{a.s.}
\end{aligned} \tag{4.19}$$

Also, by noting that  $\mathbf{Q}_n = O(\sqrt{n \log \log n})$  a.s.,  $\hat{\theta}_{n,k} = \frac{\sum_{m=1}^n X_{m,k} \zeta_{m,k} + 1}{N_{n,k} + 1}$ ,  $k = 1, \dots, d$ , and (3.1), we have

$$\begin{aligned}
\hat{\theta}_{n,k} - \theta_k &= \frac{n}{N_{n,k} + 1} \frac{1}{n} (Q_{n,k} + 1 - \theta_k) \\
&= \frac{1}{v_k} \frac{1}{n} Q_{n,k} + \left( \frac{n}{N_{n,k} + 1} - \frac{1}{v_k} \right) \frac{1}{n} Q_{n,k} + \frac{1 - \theta_k}{N_{n,k} + 1} \\
&= \frac{1}{v_k} \frac{1}{n} Q_{n,k} + O\left(\sqrt{\frac{\log \log n}{n}}\right) O\left(\sqrt{\frac{\log \log n}{n}}\right) + O\left(\frac{1}{n}\right) \\
&= \frac{1}{v_k} \frac{Q_{n,k}}{n} + O\left(\frac{1}{n}\right) \quad \text{a.s.}
\end{aligned}$$

It follows that

$$\mathbf{H}_{n+1} - \mathbf{H} = \frac{1}{v_k} \sum_{k=1}^d \frac{\partial \mathbf{H}(\mathbf{x})}{\partial x_k} \Big|_{\mathbf{x}=\boldsymbol{\theta}} \frac{Q_{n,k}}{n} + o(n^{-1/2-\delta/3}). \tag{4.20}$$

So,

$$\begin{aligned}
\mathbf{v}(\mathbf{H}_{n+1} - \mathbf{H}) &= (\hat{\boldsymbol{\theta}}_n - \boldsymbol{\theta}) \mathbf{F} + o(n^{-1/2-\delta/3}) \\
&= \frac{1}{n} \mathbf{Q}_n \text{diag}(1/v_1, \dots, 1/v_d) \mathbf{F} + o(n^{-1/2-\delta/3}) \quad \text{a.s.}
\end{aligned} \tag{4.21}$$

Then, we conclude that

$$\sum_{k=1}^n \mathbf{v}(\mathbf{H}_k - \mathbf{H}) = \sum_{k=1}^n \frac{1}{k} \mathbf{Q}_k \text{diag}(1/v_1, \dots, 1/v_d) \mathbf{F} + o(n^{1/2-\delta/3}) \quad \text{a.s.} \tag{4.22}$$

Next we will treat the terms in the left-hand side of (4.6). By (4.20),

$$\begin{aligned}
\mathbf{H}_{n+1} - \mathbf{H}_n &= \frac{1}{v_k} \sum_{k=1}^d \frac{\partial \mathbf{H}(\mathbf{x})}{\partial x_k} \Big|_{\mathbf{x}=\boldsymbol{\theta}} \left( \frac{Q_{n,k}}{n} - \frac{Q_{n-1,k}}{n-1} \right) + o(n^{-1/2-\delta/3}) \\
&= \frac{1}{v_k} \sum_{k=1}^d \frac{\partial \mathbf{H}(\mathbf{x})}{\partial x_k} \Big|_{\mathbf{x}=\boldsymbol{\theta}} \frac{\mathbf{X}_{n,k}(\zeta_{n,k} - \theta_k)}{n} + O\left(\frac{\sqrt{n \log \log n}}{n(n-1)}\right) + o(n^{-1/2-\delta/3}) \\
&= O\left(\frac{\|\boldsymbol{\xi}_n - \boldsymbol{\theta}\|}{n}\right) + o(n^{-1/2-\delta/3}) = o(n^{-1/2-\delta/3}) \quad \text{a.s.}
\end{aligned}$$

It follows that

$$\sum_{k=1}^{n-1} \|\mathbf{H}_{k+1} - \mathbf{H}_k\| = o(n^{1/2-\delta/3}) \quad \text{a.s.} \tag{4.23}$$

By (4.5),

$$\sum_{k=1}^n \|\mathbf{H}_k - \mathbf{H}\|^2 = O((\log n)(\log \log n)) \quad \text{a.s.} \quad (4.24)$$

On the other hand,  $\{\sum_{k=2}^n \mathbf{Z}_k(\mathbf{I} - \tilde{\mathbf{H}})^{-1}(\mathbf{H}_{k-1} - \mathbf{H}); n \geq 2\}$  is a martingale sequence with

$$\begin{aligned} & \left\| \sum_{k=2}^n \mathbb{E} \left[ [(\mathbf{I} - \tilde{\mathbf{H}})^{-1}(\mathbf{H}_{k-1} - \mathbf{H})]' \mathbf{Z}_k' \mathbf{Z}_k [(\mathbf{I} - \tilde{\mathbf{H}})^{-1}(\mathbf{H}_{k-1} - \mathbf{H})] \middle| \mathcal{F}_{k-1} \right] \right\| \\ &= \left\| \sum_{k=2}^n [(\mathbf{I} - \tilde{\mathbf{H}})^{-1}(\mathbf{H}_{k-1} - \mathbf{H})]' \mathbb{E}[\mathbf{Z}_k' \mathbf{Z}_k | \mathcal{F}_{k-1}] [(\mathbf{I} - \tilde{\mathbf{H}})^{-1}(\mathbf{H}_{k-1} - \mathbf{H})] \right\| \\ &\leq C \sum_{k=2}^n \|\mathbf{H}_{k-1} - \mathbf{H}\|^2 = O((\log n) \log \log n) \quad \text{a.s.} \end{aligned}$$

Hence, by the law of the iterated logarithm for martingales, we have

$$\begin{aligned} & \sum_{k=2}^n \mathbf{Z}_k(\mathbf{I} - \tilde{\mathbf{H}})^{-1}(\mathbf{H}_{k-1} - \mathbf{H}) \\ &= O\left(\sqrt{(\log n)(\log \log n) \log \log \log n}\right) \quad \text{a.s.} \end{aligned} \quad (4.25)$$

Combining (4.22)–(4.25) and (4.6), we get (4.18) immediately.

Now, by (4.2), (4.18) and Lemma 4.1, we obtain

$$\begin{aligned} (\mathbf{N}_n - n\mathbf{v})(\mathbf{I} - \tilde{\mathbf{H}}) &= \mathbf{B}_n \Sigma_1^{1/2} + \sum_{k=1}^n \frac{\mathbf{W}_k}{k} \text{diag}(\sigma_1/\sqrt{v_1}, \dots, \sigma_d/\sqrt{v_d}) \mathbf{F} + o(n^{1/2-\kappa}) \\ &= \mathbf{B}_n \Sigma_1^{1/2} + \int_0^n \frac{\mathbf{W}_x}{x} dx \text{diag}(\sigma_1/\sqrt{v_1}, \dots, \sigma_d/\sqrt{v_d}) \mathbf{F} \\ &\quad + o(n^{1/2-\kappa}) \quad \text{a.s.} \end{aligned}$$

Also,

$$\begin{aligned} \hat{\boldsymbol{\theta}}_n - \boldsymbol{\theta} &= \frac{1}{n} \mathbf{Q}_n \text{diag}(1/v_1, \dots, 1/v_d) + o(n^{-1/2-\delta/3}) \\ &= \frac{1}{n} \mathbf{W}_n \text{diag}(\sigma_1/\sqrt{v_1}, \dots, \sigma_d/\sqrt{v_d}) + o(n^{-1/2-\kappa}) \quad \text{a.s.} \end{aligned}$$

The proof is now completed.  $\square$

**A Note on the Proof of Example 2.3.** Write  $\mathbf{E} = (1, -1)'(1, -1)$ . Note that  $v_1 = \frac{q_2}{q_1+q_2}$ ,  $v_2 = \frac{q_1}{q_1+q_2}$ ,  $\sigma_1^2 = p_1 q_1$ ,  $\sigma_2^2 = p_2 q_2$ ,

$$\mathbf{H} = \frac{1}{q_1 + q_2} \begin{pmatrix} q_2 & q_1 \\ q_2 & q_1 \end{pmatrix} = \mathbf{1}' \mathbf{v}.$$

So,  $\tilde{\mathbf{H}} = \mathbf{H} - \mathbf{1}'\mathbf{v} = \mathbf{0}$  and  $\Sigma = \Sigma_1 = \frac{q_1 q_2}{(q_1 + q_2)^2} \mathbf{E}$ . Also,

$$\begin{aligned} \left. \frac{\partial \mathbf{H}(\mathbf{x})}{\partial x_1} \right|_{\mathbf{x}=(p_1, p_2)} &= \frac{q_2}{(q_1 + q_2)^2} \begin{pmatrix} 1 & -1 \\ 1 & -1 \end{pmatrix} \quad \text{and} \quad \left. \frac{\partial \mathbf{H}(\mathbf{x})}{\partial x_2} \right|_{\mathbf{x}=(p_1, p_2)} \\ &= \frac{q_1}{(q_1 + q_2)^2} \begin{pmatrix} -1 & 1 \\ -1 & 1 \end{pmatrix}. \end{aligned}$$

It follows that

$$\begin{aligned} \mathbf{F} &= \frac{1}{q_1 + q_2} (q_2, -q_1)' (1, -1) \quad \text{and} \\ \Sigma_{\dagger} &= \mathbf{F}' \text{diag}(\sigma_1^2/v_1, \sigma_2^2/v_2) \mathbf{F} = \frac{q_1 q_2 (p_1 + p_2)}{(q_1 + q_2)^3} \mathbf{E}. \end{aligned}$$

Then

$$\Lambda = \Sigma + 2\Sigma_{\dagger} = \frac{q_1 q_2 (2 + p_1 + p_2)}{(q_1 + q_2)^3} \mathbf{E}.$$

The proof is completed.  $\square$

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## References

- [1] Z.D. Bai, Y.M. Chen, F. Hu, Z.Y. Lin, Adaptive designs based on Markov chains, *Chinese J. Biomath.* 18 (2003) 597–609.
- [2] Z.D. Bai, F. Hu, Asymptotic theorem for urn models with nonhomogeneous generating matrices, *Stochastic Process. Appl.* 80 (1999) 87–101.
- [3] Z.D. Bai, F. Hu, Asymptotics in randomized urn models, *Ann. Appl. Probab.* 15 (2005) 914–940.
- [4] Z.D. Bai, F. Hu, L. Shen, An adaptive design for multi-arm clinical trials, *J. Multi. Anal.* 81 (2002) 1–18.
- [5] P. Hall, C.C. Heyde, *Martingale Limit Theory and its Applications*, Academic Press, London, 1980.
- [6] D.G. Hoel, M. Sobel, Comparison of sequential procedures for selecting the best binomial population, *Proceedings of the Sixth Berkeley Symposium on Mathematical Statistics and Probabilities*, vol. IV, 1972, pp. 53–69.
- [8] F. Hu, W.F. Rosenberger, Optimality, variability, power: evaluating response-adaptive randomization procedures for treatment comparisons, *J. Amer. Statist. Assoc.* 98 (2003) 671–678.
- [9] V. Melfi, C. Page, Variability in adaptive designs for estimation of success probabilities, in: N. Flournoy, W.F. Rosenberger, W.K. Wong (Eds.), *New Developments and Applications in Experimental Design*, Institute of Mathematical Statistics, Hayward, 1998, pp. 106–114.
- [10] V.F. Melfi, C. Page, Estimation after adaptive allocation, *J. Statist. Plann. Inference* 87 (2000) 353–363.
- [11] V.F. Melfi, C. Page, M. Geraldes, An adaptive randomized design with application to estimation, *Canad. J. Statist.* 29 (2001) 107–116.
- [12] W.F. Rosenberger, N. Stallard, A. Ivanova, C.N. Harper, M.L. Ricks, Optimal adaptive designs for binary response trials, *Biometrics* 57 (2001) 909–913.
- [13] R.T. Smythe, Central limit theorems for urn models, *Stochastic Process. Appl.* 65 (1996) 115–137.

- [14] R.T. Smythe, W.F. Rosenberger, Play-the-winner designs, generalized Pólya urns, and Markov branching processes, in: N. Flournoy, W.F. Rosenberger (Eds.), *Adaptive Designs*, Institute of Mathematical Statistics, Hayward, CA, 1995, pp. 13–22.
- [15] W.F. Stout, *Almost Sure Convergence*, Academic Press, New York, 1974.
- [16] L.J. Wei, The generalized Polya's urn design for sequential medical trials, *Ann. Statist.* 7 (1979) 291–296.
- [17] L.J. Wei, S. Durham, The randomized play-the-winner rule in medical trials, *J. Amer. Statist. Assoc.* 73 (1978) 840–843.
- [18] M. Zelen, Play the winner rule and the controlled clinical trial, *J. Amer. Statist. Assoc.* 64 (1969) 131–146.
- [19] L.X. Zhang, Strong approximations of martingale vectors and their applications in Markov-Chain adaptive designs, *Acta Math. Appl. Sinica* 20 (2) (2004) 337–352.